

AMENDMENTS TO THE CLAIMS

This Listing of Claims will replace all prior versions, including listings, of claims in the application.

Listing of Claims

Claim 1 (currently amended): A substantially pure conotoxin peptide having the general formula I:

Xaa-Xaa₀-Xaa₁-Cys-Cys-Gly-Xaa₂-Xaa₃-Xaa₄-Cys-Xaa₅-Xaa₆-Cys-Xaa₇ (SEQ ID NO:1),
wherein Xaa is *des*-Xaa, Asn, Gln or pyro-Glu;

Xaa₀ is *des*-Xaa₀, Gly, Ala, Glu, γ -carboxy-Glu (Gla) Asp, Asn, Ser, Thr, g-Asn (where g is glycosylation), g-Ser or g-Thr;

Xaa₁ is Val, Ala, Gly, Leu, Ile, Ser, Thr, g-Asn, g-Ser or g-Thr;

Xaa₂ is Phe, Tyr, meta-Tyr, ortho-Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, Trp (D or L), neo-Trp, halo-Trp (D or L), any non-natural **synthetic** aromatic amino acid, an aliphatic amino acid bearing linear or branched saturated hydrocarbon chains or a non-natural derivatives of the aliphatic amino acid;

Xaa₃ is Lys, Arg, homolysine, homoarginine, ornithine, nor-Lys, His, N-methyl-Lys, N,N'-dimethyl-Lys, N,N',N''-trimethyl-Lys, any non-natural **synthetic** basic amino acid, Ser, Thr, g-Ser, g-Thr or any non-natural hydroxylated **synthetic** residue;

Xaa₄ is an aliphatic amino acid bearing linear or branched saturated hydrocarbon chains or a non-natural derivative of the aliphatic amino acid, Met, Phe, Tyr, meta-Tyr, ortho-Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, Trp (D or L), neo-Trp, halo-Trp (D or L) or any non-natural **synthetic** aromatic amino acid;

Xaa₅ is His, Ser, Thr, g-Ser, g-Thr, an aliphatic amino acid bearing linear or branched saturated hydrocarbon chains, a non-natural derivative of the aliphatic amino acid, Phe, Tyr, meta-

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Tyr, ortho-Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, Trp (D or L), neo-Trp, halo-Trp (D or L) or a non-natural synthetic aromatic amino acid;

Xaa₆ is Pro, hydroxy-Pro (Hyp) or g-Hyp;

Xaa₇ is *des*-Xaa₇, Gly, Ala, Lys, Arg, homolysine, homoarginine, ornithine, nor-Lys, His, N-methyl-Lys, N,N'-dimethyl-Lys, N,N',N''-trimethyl-Lys or any non-natural synthetic basic amino acid; and

the C-terminus contains a free carboxyl group or an amide group.

Claim 2 (previously presented): The substantially pure conotoxin peptide of claim 1 selected from the group consisting of:

Asn-Gly-Val-Cys-Cys-Gly-Xaa₁-Xaa₂-Leu-Cys-His-Xaa₃-Cys (SEQ ID NO:2); and

Gly-Val-Cys-Cys-Gly-Xaa₁-Xaa₂-Leu-Cys-His-Xaa₃-Cys (SEQ ID NO:3);

wherein Xaa₁ is Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr; Xaa₂ is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa₃ is Pro or hydroxy-Pro; and the C-terminus contains a carboxyl or amide group.

Claim 3 (original): The substantially pure conotoxin peptide of claim 2, wherein Xaa₁ is Tyr.

Claim 4 (original): The substantially pure conotoxin peptide of claim 2, wherein Xaa₂ is Lys.

Claim 5 (original): The substantially pure conotoxin peptide of claim 2, wherein Xaa₃ is hydroxy-Pro.

Claim 6 (canceled).

Claim 7 (previously presented): The substantially pure conotoxin peptide of claim 2, wherein Xaa₁ is Tyr, Xaa₂ is Lys, and Xaa₃ is hydroxy-Pro.

Claim 8 (original): The substantially pure conotoxin peptide of claim 2, wherein halo is iodine.

Claim 9 (original): The substantially pure conotoxin peptide of claim 8, wherein Xaa₃ is mono-iodo-Tyr.

Claim 10 (original): The substantially pure conotoxin peptide of claim 8, wherein Xaa₃ is di-iodo-Tyr.

Claim 11 (canceled).

Claim 12 (currently amended): A substantially pure conotoxin peptide derivative comprising the peptide of claim 2, wherein at least one amino acid residue is substituted, said substitution being selected from the group consisting of an Xaa₂ residue substituted by Arg, ornithine, homoarginine, nor-Lys, or any non-natural **synthetic** basic amino acid; a Tyr residue substituted with any non-natural **synthetic** aromatic containing amino acid; a Ser residue substituted with Thr or any non-natural **synthetic** hydroxy containing amino acid; a Thr residue substituted with Ser or any synthetic hydroxy containing amino acid; a Phe residue substituted with any non-natural **synthetic** aromatic amino acid; a Trp residue substituted with any non-natural **synthetic** aromatic amino acid; an Asn residue glycosylated; a Ser residue glycosylated; a Thr residue glycosylated; a Hyp residue glycosylated; a Cys residue in D or L configuration; a Cys residue substituted with homocysteine (D or L); a Tyr residue substituted with the 3-hydroxyl or 2-hydroxyl isomers (meta-Tyr or ortho-Tyr, respectively) and corresponding O-sulpho- and O-phospho-derivatives; an acidic amino acid residue

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substituted with any non-natural ~~synthetic~~ acidic amino acid; a pair of Cys residues replaced pairwise with isoteric lactam or ester-thioether replacements; and an aliphatic amino acid substituted by synthetic derivatives bearing non-natural aliphatic branched or linear side chains C_nH_{2n+2} up to and including $n=8$.

Claim 13 (original): The substantially pure conotoxin peptide of claim 2, wherein said peptide has the sequence set forth in SEQ ID NO:2, wherein Xaa_1 is Tyr, Xaa_2 is Lys and Xaa_3 is hydroxy-Pro.

Claim 14 (original): The substantially pure conotoxin peptide of claim 2, wherein said peptide has the sequence set forth in SEQ ID NO:3, wherein Xaa_1 is Tyr, Xaa_2 is Lys and Xaa_3 is hydroxy-Pro.

Claims 15-18 (canceled).

Claim 19 (original): A method for inducing analgesia in a mammal which comprises administering a therapeutically effective amount of a conotoxin peptide of claim 1.

Claim 20 (original): The method of claim 19, wherein said administration comprises using a delivery means selected from the group consisting of a pump, microencapsulation, a continuous release polymer implant, macroencapsulation, naked or unencapsulated cell grafts, injection and oral administration.

Claim 21 (original): The method of claim 20, wherein administration is intrathecal injection.

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Claim 22 (original): The method of claim 20, wherein administration is intracerebroventricular injection.

Claim 23 (original): The method of claim 20, wherein administration is by pump.

Claim 24 (previously presented): The method of claim 20, wherein the amount of conotoxin peptide administered is between about 0.001 mg/kg to about 250 mg/kg.

Claim 25 (original): The pharmaceutical composition comprising a therapeutically effective amount of the conotoxin peptide of claim 1 or a pharmaceutically acceptable salt or solvate thereof and a pharmaceutically acceptable carrier.

Claim 26 (original): The composition of claim 25 which further comprises one or more drugs useful in the treatment of pain.

Claims 27-28 (canceled).

Claim 29 (previously presented): An isolated conotoxin propeptide having the amino acid sequence set forth in SEQ ID NO:12.

Claims 30-31 (canceled).

Claim 32 (previously presented): The substantially pure conotoxin peptide of claim 1, wherein said aliphatic amino acid bearing linear or branched saturated hydrocarbon chains is Leu (D or L), Ile, or Val.

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Claim 33 (previously presented): The substantially pure conotoxin peptide derivative of claim 12, wherein said synthetic acidic amino acid is a tetrazolyl derivative of Gly or Ala.

Claim 34 (previously presented): The substantially pure conotoxin peptide derivative of claim 12, wherein said isoteric lactam or esterthioether replacements are Ser/(Glu or Asp), Lys/(Glu or Asp), or Cys/Ala combinations.